

WHAT IS CLAIMED IS:

1. A method for detecting the presence or absence of a genetic variation at a polymorphic site in a nucleic acid analyte in a sample, comprising the steps of:

(a) preparing labeled amplicons from the nucleic acid analyte contained in the sample;
(b) contacting, under hybridization conditions, the labeled amplicons with a plurality of first and second differential hybridization probes, wherein wild type complexes are formed between each first differential hybridization probe and a single labeled amplicon having a wild type sequence at the polymorphic site, and variant complexes are formed between each second differential hybridization probe and a single labeled amplicon having a variant sequence at the polymorphic site;

(c) contacting, under hybridization conditions, any wild type complexes and variant type complexes formed in step (b) with a plurality of first and second capture probes, wherein a captured wild type complex having a first detectable signal is formed between each wild type complex and a single first capture probe, and a captured variant complex having a second detectable signal is formed between each variant sequence and a single second capture probe;

(d) detecting and counting any captured wild type complexes and captured variant complexes formed in step (c); and

(e) determining the presence or absence of the genetic variation by comparing the relative amounts of the captured wild type and captured variant complexes detected in step (d), wherein a greater amount of captured wild type complexes is indicative of the absence of the genetic variation and a greater amount of captured variant complexes is indicative of the presence of the genetic variation.

2. The method of claim 1, wherein each first differential hybridization probe is comprised of a first capture sequence portion and a region that is complementary to the polymorphic site corresponding to the wild type sequence, and wherein each second differential hybridization probe is comprised of a second capture sequence portion and a region that is complementary to the polymorphic site corresponding to the variant sequence.

3. The method of claim 2, wherein each of the first and second differential hybridization probes has a spacer portion.

4. The method of claim 3, wherein each spacer portion of the first and second differential hybridization probes is located between the capture sequence portion and the region that is complementary to the polymorphic site.

5. The method of claim 2, wherein each first capture probe is (i) comprised of a region that is complementary to the first capture sequence portion and (ii) attached to a single solid substrate that provides the first detectable signal, and each second capture probe is (i) comprised of a region that is complementary to the second capture sequence portion and (ii) attached to a single separate solid substrate that provides the second detectable signal.

6. The method of claim 1, wherein the first and second detectable signals are provided by moieties selected from the group consisting of fluorescers, chemiluminescers, dyes, biotin, haptens, enzymes, enzyme substrates, enzyme cofactors, enzyme inhibitors, enzyme subunits, metal ions, electron-dense reagents, and radioactive isotopes.

7. The method of claim 6, wherein the first and second detectable signals are provided by one or more fluorescent dyes.

8. The method of claim 7, wherein the first and second detectable signals are provided by two fluorescent dyes.

9. The method of claim 8, wherein the first detectable signal is provided by a ratio of the two different fluorescent dyes and the second detectable signal is produced by a different ratio of the two different fluorescent dyes.

10. The method of claim 1, wherein step (c) is performed by running the captured wild type and variant complexes through a flow cytometer designed to detect and count both the detectable signals and the label of the labeled amplicon.

11. The method of claim 10, wherein step (c) is performed by running the captured wild type and variant complexes through a flow cytometer designed to detect and count the first and second detectable signals, and the label of the labeled amplicon, wherein detection of the label of the labeled amplicon and

the first detectable signal is indicative of a captured wild type complex and wherein detection of the label of the labeled amplicon and the second detectable signal is indicative of a captured variant complex.

12. The method of claim 1, wherein the labeled amplicons are PCR products produced via PCR synthesis with labeled primers.

13. The method of claim 12, wherein the labeled primers are biotinylated primers.

14. The method of claim 1, wherein the labeled amplicons are directly or indirectly labeled with a moiety selected from the group consisting of fluorescers, chemilumescers, dyes, biotin, haptens, enzymes, enzyme substrates, enzyme cofactors, enzyme inhibitors, enzyme subunits, metal ions, electron-dense reagents, and radioactive isotopes.

15. The method of claim 1, wherein the sample is obtained from a patient.

16. The method of claim 1, wherein the genetic variation is a single nucleotide polymorphism.

17. The method of claim 1, wherein the genetic variation is a cluster of polymorphisms.

18. The method of claim 1, wherein the genetic variation is associated with a genetic disorder.

19. The method of claim 1, wherein the genetic variation is associated with allelic variation.

20. The method of claim 1, wherein the genetic variation is associated with an exon sequence.

21. The method of claim 1, wherein the genetic variation is associated with an intron sequence.

22. The method of claim 1, wherein the genetic variation is associated with a genetic subtype.

23. The method of claim 1, wherein the nucleic acid analyte is obtained from a gene belonging to a patient.

24. The method of claim 1, wherein the nucleic acid analyte belongs to the gene of an infectious agent selected from the group consisting of viral, bacterial, and fungal organisms.

25. The method of claim 1, used to predict phenotype.

26. The method of claim 1, in multiplex form wherein a plurality of genetic variations is detected through use of a plurality of different differential hybridization probes and capture probes.

27. The method of claim 24, used to detect clusters of polymorphisms.

28. An assay kit for detecting the presence or absence of a genetic variation at a polymorphic site in a nucleic acid analyte in a sample, comprising:

(a) a plurality of first differential hybridization probes each comprised of a first capture sequence portion and a region that is complementary to the polymorphic site corresponding to a wild type sequence;

(b) a plurality of second differential hybridization probes each comprised of a second capture sequence portion different from the first capture sequence portion and a region that is complementary to the polymorphic site corresponding to a variation sequence;

(c) a plurality of first solid substrates each (i) comprised of an attached first capture probe complementary to the first capture region and (ii) having a first detectable signal; and

(d) a plurality of second solid substrates each (i) comprised of an attached second capture probe complementary to the second capture region and (ii) having a second detectable signal.

29. The assay kit of claim 28, wherein each first and second solid substrate is a bead.

30. The assay kit of claim 28, wherein the first and second detectable signals are provided by one or more fluorescent dyes.

31. The assay kit of claim 30, wherein the first and second detectable signals are provided by two dyes.

32. The assay kit of claim 31, wherein the first detectable signal is provided by a ratio of the two different dyes and the second detectable signal is produced by a different ratio of the two different dyes.

33. The assay kit of claim 28, further comprising a polymerase for amplifying nucleic acids.
34. The assay kit of claim 28, further comprising primers for carrying out PCR.
35. The assay kit of claim 34, wherein the primers are labeled.
36. The assay kit of claim 35, wherein the labeled primers are biotinylated primers.
37. The assay kit of claim 28, further comprising instructions for carrying out an assay for detecting the presence or absence of a genetic variation.